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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/576,356 | 12/11/2006 | Richard R. Bott | DOG 0101 PA/35319.68 | 9374 |

23368 7590 04/14/2010

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| EXAMINER | |
|---|---|
| ASHBY, TANIA L | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1611 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 04/14/2010 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/576,356 | BOTT ET AL. | |
| | Examiner | Art Unit | |
| | TANIA ASHBY | 1611 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *26 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *72 and 74-91* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *72 and 74-91* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *July 24, 2009 and February 10, 2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Acknowledgement is made to Applicant's response and amendments dated October 26, 2009. Claims 72 and 74-91 are the subject of this office action.

### *Information Disclosure Statement*

The information disclosure statement (IDS) submitted on July 24, 2009 was noted and the submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the examiner has considered the information disclosure statement.

The information disclosure statement (IDS) submitted on February 10, 2010 was noted and the submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the examiner has considered the information disclosure statement.

In regards to the information disclosure statement dated September 10, 2008, the examiner has considered the non-patent citation of "Dow Corning Acrylic Adhesives for Healthcare (2004), now present in the file wrapper as of July 24, 2009.

### *Rejections Withdrawn*

The rejection of claim 90 under 35 U.S.C. 101 and 112 is withdrawn in light of the amendment to the claim.

The rejection of claim 79 under 35 U.S.C. 112 is also withdrawn in light of the amendment to the claim.

The 35 U.S.C. 102(b) rejection of claims 72-79, 81, 83-84 and 87-88 over Foldvari et al. is withdrawn upon further consideration by the examiner.

The 35 U.S.C. 103(a) rejection of claim 89 over Foldvari et al. in view of Mackles is withdrawn upon further consideration by the examiner.

The 35 U.S.C. 103(a) rejection of claims 80, 82 and 85-86 over Foldvari in view of Bott is withdrawn upon further consideration by the examiner.

***New Grounds of Rejection***

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 72-79, 81, 83-84 and 87-88 is rejected under 35 U.S.C. 103(a) as being unpatentable over Foldvari et al. (U.S. Pat. 5,993,852, issued November 30, 1999) in view of Kosal (U.S. 6,545,086, issued April 8, 2003).**

The Foldvari et al. reference teaches a composition that includes an oil-in-water (O/W) emulsion for transdermal administration (abstract). The Foldvari et al. reference also teaches a transdermal device for administration of the composition (column 2, lines 41-54).

Foldvari does not appear to explicitly teach the silicone component contained within the emulsion.

The Kosal reference (Kosal) teaches a pressure sensitive adhesive emulsion comprising a silicone pressure sensitive adhesive where the silicone phase is emulsified in a continuous water phase (abstract). Kosal further teaches an oil-in-water emulsion formed by an inversion procedure (column 4, lines 55-65) where the silicone pressure sensitive adhesive emulsion can be used in personal care applications and in medical applications such as transdermal drug delivery patches or to hold active materials (column 5, lines 14-30).

It would have been prima facie obvious to one having ordinary skill in the art at the time of the invention to combine the teachings of Foldvari with the silicone pressure sensitive adhesive emulsion taught by Kosal. One would have been motivated to do so

because Kosal teaches that the pressure sensitive adhesive emulsion delivers advantageous performance properties such as controlled tack. Further, Kosal suggests using the silicone pressure sensitive adhesive emulsion in a medical application such as a transdermal patch where the pressure sensitive adhesive emulsion is able to hold an active material to the skin surface (column 5, lines 14-30).

Regarding claim 72, the Foldvari et al. reference teaches a composition comprised of an oil-in-water emulsion that additionally includes an immunogen (i.e. protein, column 4, lines 15-16) incorporated into the emulsion. The emulsion is disclosed in column 5, lines 64-67 as having a hydrophilic solvent (i.e. being substantially free of lipophilic solvent). The membrane and the reservoir taught in Figure 3A of the Foldvari et al. reference together form the controlled release layer of the composition. The composition is furthermore taught in the abstract to be administered transdermally (i.e. topically to the skin). Although Foldvari et al. does not disclose the emulsion as being formed by mechanical inversion of a water-in-oil emulsion, the process by which the composition is made is irrelevant where the composition disclosed by the prior art is structurally equivalent to the composition that Applicant is claiming. In the instant case, the formation of the emulsion by mechanical inversion does not afford any structural differences to the claimed composition (i.e. the composition is comprised of identical elements) and therefore the composition taught by the prior art anticipates the claim.

Regarding the newly incorporated limitation of claim 72 and claims 83-84, Kosal teaches a pressure sensitive adhesive emulsion comprising a silicone pressure

sensitive adhesive where the silicone phase is emulsified in a continuous water phase (abstract) and further teaches teaches an oil-in-water emulsion formed by an inversion procedure (column 4, lines 55-65) where the silicone pressure sensitive adhesive emulsion can be used in personal care applications and in medical applications such as transdermal drug delivery patches or to hold active materials (column 5, lines 14-30). Further, Foldvari teaches the active agent (i.e., immunogen) as being able to be entrapped in the water phase (hydrophilic phase) of the oil-in-water emulsion depending on the physiochemical properties of the immunogen (column 4, lines 57-65). The reference furthermore details the hydrophilic phase as being prepared in Example 1 by mixing components including propylene glycol (carrier) and water.

Regarding claim 74, column 6, line 62 of the Foldvari et al. reference teaches the inclusion of a surfactant in the emulsion.

Regarding claim 75, column 5, lines 64-67 of the Foldvari et al. reference teaches numerous carriers including propylene glycol.

Regarding claim 76, column 14, lines 22-26 of the Foldvari et al. reference teaches the propylene glycol (carrier) in solution with water.

Regarding claims 77-79, the protein taught in Foldvari et al. is a natural enzyme, more specifically egg lysozyme (a hydrolase) (column 13, lines 7-9).

Regarding claim 81, the Foldvari et al. reference discloses a skin permeation enhancer in column 8, lines 19-20 that has the ability to enhance the penetration of the entrapped antigen (i.e. active). Although the reference does not specifically state that the penetration enhancer is a dispersing agent, absent any other explicit definition

provided by Applicant in the specification, dispersing agent is interpreted to mean a substance that facilitates the distribution of the active agent. A skin permeation enhancer, like the one taught by Foldvari et al., would necessarily function as such.

Regarding claim 87, the controlled release layer is formed from the reservoir 42 and the outer membrane 46 that retains the formulation within the reservoir in Figure 3A of the Foldvari et al. reference and additionally in column 9, lines 15-23. The adhesive layer 50 is also set forth in Figure 3A and is adjacent to the controlled-release layer (comprising both the membrane and the reservoir). Figure 3A also shows an additional backing layer 42.

Regarding claim 88, Figure 3C of the Foldvari et al. reference teaches a third transdermal device wherein the reservoir 82 is composed of an absorbent sponge or a permeable polymer (also considered the controlled release layer), that is in direct contact with the skin (column 10, lines 10-13). The transdermal device furthermore comprises an adhesive layer 86 and an additional layer 88 (backing layer) where the additional layer is adjacent the adhesive layer but spaced from the controlled release layer.

**Claim 89 is rejected under 35 U.S.C. 103(a) as being unpatentable over Foldvari et al. (U.S. Pat. 5,993,852, issued November 30, 1999) in view of Kosal (U.S. 6,545,086, issued April 8, 2003), as applied to claims 72-79, 81, 83-84 and 87-**

**88 above, and further in view of Mackles et al. (U.S. Pat. 5,178,881, issued January 12, 1993).**

The Foldvari et al. reference teaches a composition that includes an oil-in-water (O/W) emulsion for transdermal administration (abstract). The Foldvari et al. reference also teaches a transdermal device for administration of the composition (column 2, lines 41-54).

The Foldvari et al. reference does not teach the controlled release layer (formed from the controlled release composition) as being free of water.

The Mackles et al. reference teaches anhydrous topical compositions that dry rapidly on contact (title).

Regarding claim 89, the Mackles et al. reference teaches anhydrous topical bases that function as delivery systems for medications (column 1, lines 24-25) further in the form of an oil-in-water emulsion (column 1, lines 43-47).

It would have been obvious to a person having ordinary skill in the art, at the time of invention, to be motivated to combine the teachings of the Foldvari et al. reference with the anhydrous feature of the topical composition taught by Mackles et al. because the Mackles et al. reference discusses several disadvantages of the presence of water in the composition. More specifically, in column 1, lines 67-68, Mackles et al. teaches that the presence of water can result in active ingredient instability. This would be particularly disadvantageous in the instant invention because the instant invention is drawn to a controlled release composition that in some embodiments comprises an

active ingredient. It is especially important in controlled release systems that the active ingredient be stable to ensure more optimal drug delivery.

***Response to Arguments***

Although a new grounds of rejection has been issued, Applicant's arguments as they relate to Mackles may still be pertinent and thus are addressed below.

Applicant's arguments filed October 26, 2009 have been fully considered but they are not persuasive.

Applicant argues that Mackles teaches away from the use of an emulsion by teaching that emulsions are inherently unstable (pages 10-11 of response).

This is found unpersuasive because Mackles does not explicitly teach away from the use of oil-in-water emulsions. For example, Mackles teaches the advantages of these systems, such as rapid absorption with reduced stickiness and cosmetic elegance (column 1, lines 43-52). Mackles may teach that these systems have negatives such as fleeting action, undesirable wetness, microbiological problems requiring preservative use and inherent instability (column 1, line 52 to column 2, line 5), but Mackles teaches that these problems *are a result of the presence of water*.

For example, Mackles states, "Newer washable systems are more easily removed so their action is fleeting," "they are perceived as wet and cold feeling and require time for absorption to dry," "water sometimes results in active ingredient instability," and finally, "water presents microbiological problems requiring the use of preservatives."

The skilled artisan would interpret washable systems being easily removed and being perceived as wet and requiring drying time because of the presence of water.

Mackles proposes an elimination of these problems by eliminating water (i.e. making an anhydrous base.) See column 2, lines 16-22 where Mackles states, "Since water and emulsifiers are not required, irritation is eliminated, instability of active ingredients is avoided, wetness and slow drying are eliminated." Further, "preservation problems, even in the absence of preservatives, are absent." Note that the only problem associated with the use of emulsifiers is that they may "sometimes be irritating to the skin (column 1, lines 62-63)" but that all the other nuances acknowledged by Mackles are attributed to the presence of water. Taking Mackles teachings as a whole, it would have been obvious to the skilled artisan at the time of the invention to remove the water from an emulsion system after the formation of the controlled release layer because Mackles teaches numerous problems associated with the presence of water. The removal of water as taught by Mackles would eliminate problems in the instant invention and thus the skilled artisan would be motivated to do so to improve the properties of the instant invention. Therefore, Mackles does not teach away from the use of emulsion systems, but teaches away from the presence of water in a system, giving motivation to remove such an element as it is the cause of instability and preservation problems.

**Claims 80, 82 and 85-86 are rejected under 35 U.S.C. 103(a) as being unpatentable over Foldvari et al. (U.S. Pat. 5,993,852, issued November 30, 1999)**

**in view of Kosal (U.S. 6,545,086, issued April 8, 2003), as applied to claims 72-79, 81, 83-84 and 87-88 above, and further in view of Bott et al. (U.S. 2003/0180281, filed March 10, 2003) as evidenced by Kanios et al. (U.S. Pat. 6,337,086, issued January 8, 2002).**

The Foldvari et al. reference teaches a composition that includes an oil-in-water (O/W) emulsion for transdermal administration (abstract). The Foldvari et al. reference also teaches a transdermal device for administration of the composition (column 2, lines 41-54).

The Foldvari et al. reference does not teach any of the specific enzymes recited in claim 80, nor a dispersing agent comprised of a silicone-based surfactant, nor a pressure sensitive adhesive comprising the reactant product of claim 85 or the silicate resin further defined in claim 86.

The Bott et al. reference teaches a topical preparation containing a silicone matrix, a hydrophilic carrier such as propylene glycol, polyethylene glycol, poloxamer, glycerin, alcohol, polyhydric alcohol, and water, and combinations thereof, and at least one active agent for release from the preparation ([0060], [0008] and claim 11), which forms oil-in-water or water-in-oil emulsion [0008].

Regarding claim 80, the Bott et al. reference teaches proteases such as protease A or protease B in embodiment [0049] of the invention.

Regarding claims 82 and 85-86, the Bott et al. reference teaches a silicone matrix that is selected from high molecular weight polydimethylsiloxanes, loosely or lightly cross-linked silicone elastomers, fillerless elastomers, cellular elastomers,

silicone rubbers, silicone pressure sensitive adhesives, and combinations thereof. It discloses the silicone matrix may be comprised of a silicone pressure sensitive adhesive (silicone PSA), such as a silicate resin in silicone polymers, which includes the reaction product of a hydroxyl endblocked polydimethylsiloxane polymer and a hydroxyl functional silicate resin ([0041], evidenced by US patent 6,337,086, the disclosure of which is incorporated by reference for their teaching of silicone PSAs for use in US Patent Publication 2003/0180281).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the silicone component and the proteases (more specifically protease A or protease B) taught by Bott et al. for the emulsion taught by Foldvari et al. with a reasonable expectation of success because the Bott et al. reference teaches that silicone components aid controlled and sustained release of active agents (embodiment [0002]) and furthermore teaches that wound dressings comprising a biochemical agent and a silicone matrix accelerate the healing of the skin (embodiment [0004]). With regard to the specific enzymes (i.e. proteases), embodiments [0007 and 0051] of the Bott et al. reference also suggest that the silicone matrix will be successful in the release of such proteases and that the proteases aid in general wound healing as well as clotting formation or removal. This feature is particularly advantageous to the instant invention because the instant invention is drawn to a controlled release composition for topical application and in some embodiments, a multi-layer dressing that could function as a wound dressing.

***Response to Arguments***

Although a new grounds of rejection has been issued, Applicants' arguments as they pertain to Bott may still be relevant to the new grounds of rejection and thus are addressed below.

Applicant's arguments filed October 26, 2009 have been fully considered but they are not persuasive.

Applicant argues that Bott does not teach or suggest a hydrophobic phase comprising a silicone component because the hydrophilic carrier containing an active agent is dispersed throughout a silicone matrix. This is unpersuasive because the currently pending claims are drawn to an oil-in-water emulsion which is necessarily a dispersion of oil droplets in a continuous water phase. Also see [0026] of Bott which defines an emulsion as it relates to the invention. The fact that the hydrophilic carrier and active agent are dispersed within the silicone matrix does not suggest that the silicone matrix is not a hydrophobic phase as is argued by Applicant (page 12 of response). Further note that the techniques associated with the formulation of oil-in-water emulsions and water-in-oil emulsions are routine to the skilled artisan. Further note that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, the rejection of claims 80, 82 and 85-86 is over the prima facie obvious combination of Foldvari, Kosal and Bott, where Foldvari and Bott both teach emulsions having a hydrophobic and hydrophilic phase. Also note that the skilled

artisan would have readily been able to determine the constitution of hydrophobic and hydrophilic phases at the time of the invention using techniques routine to the art and further based upon the solubility profiles of the components to be emulsified.

***Conclusion***

No claims are currently allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TANIA ASHBY whose telephone number is (571)270-1348. The examiner can normally be reached on Monday through Friday, 7:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571) 272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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